Control of thermoregulatory sweating during exercise in the heat

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SAWKA, MICHAEL N., RICHARD R. GONZALEZ, ANDREW J. YOUNG, RICHARD C. DENNIS, C. ROBERT VALERI, AND KENT B. PANDOLF. *Control of thermoregulatory sweating during exercise in the heat.* Am. J. Physiol. 257 (Regulatory Integrative Comp. Physiol. 26): R311–R316, 1989.—The purposes of this study were the following: *1*) to determine whether erythrocyte infusion alters the control of thermoregulatory sweating and *2*) to demonstrate how increases and decreases of both plasma tonicity and blood volume influence the thermoregulatory control parameters of threshold temperature and sweating sensitivity. Six non-heat-acclimated and five heat-acclimated males attempted heat stress tests (HSTs) both before and shortly after (48–96 h) autologous erythrocyte infusion. The non-heat-acclimated subjects were euhydrated for both HSTs, whereas the heat-acclimated subjects were studied in a euhydrated and a hypohydrated (−5% body wt) condition both pre- and postinfusion (500 ml of solution containing ~60% hematocrit of autologous erythrocytes). The HSTs consisted of treadmill exercise (335 $W \cdot m^{-2}$) in a hot (35°C, 45% relative humidity) environment, and esophageal temperature and local sweating rate were continuously measured during 25 min of exercise. These experiments resulted in a matrix of conditions where both plasma tonicity and blood volume were increased or decreased relative to control conditions (euhydration, preinfusion). The findings concerning thermoregulatory sweating during exercise in the heat were summarized as follows: *1*) acute polycythemia decreases the threshold temperature and increases the sweating sensitivity, *2*) both threshold temperature and sweating sensitivity are increased or decreased from control levels dependent on the combined influence of plasma tonicity and blood volume, and *3*) equations are presented that describe how plasma tonicity and blood volume alter threshold temperature and sweating sensitivity values.

acute polycythemia; dehydration; erythrocyte infusion; hypervolemia; hypohydration; hypovolemia; hyperosmolality; sweating sensitivity; temperature regulation; thermoregulation; threshold temperature

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ACUTE POLYCYTHEMIA has been reported to reduce thermal strain and improve exercise performance in the heat for both non-heat-acclimated (23) and heat-acclimated (26) humans. That research, however, does not address the question of whether acute polycythemia alters the thermoregulatory control system. In this paper, we determined whether the control parameters of threshold temperature and sweating sensitivity were modified by erythrocyte infusion. We also evaluated how these thermoregulatory control parameters were altered by the singular and combined effects of changes in plasma tonicity and changes in blood volume. Plasma tonicity and blood volume are believed to be the primary physiological variables that can modify the thermoregulatory effector responses (9, 28). Fortuitously, the following experiments resulted in a matrix of conditions in which both plasma tonicity and blood volume were increased and decreased relative to control conditions (euhydrated, preinfusion). As a result, we were provided an opportunity to gain insight into the control of thermoregulatory sweating during exercise-heat stress.

The purposes of this study were the following: *1*) to determine whether erythrocyte infusion alters the control of thermoregulatory sweating and *2*) to demonstrate how increases and decreases of both plasma tonicity and blood volume influence the thermoregulatory sweating control parameters of threshold temperature and sweating sensitivity.

METHODS

The data reported in this paper were collected as part of a comprehensive research effort concerning erythrocyte infusion and exercise performance. The data presented were collected during the same experiments that resulted in two previous studies (23, 26). Only the methodology directly related to the present data are provided; additional methodological information can be obtained from the previously published studies (23, 26).

Subjects. Eleven male subjects participated in these experiments; six subjects were non-heat acclimated, and five subjects were heat acclimated. The non-heat-acclimated subjects had a mean (±SD) age of 30 ± 7 yr, body surface area of 2.0 ± 0.2 m^2, percent body fat of 15 ± 5, and maximal O_2 uptake of 54 ± 5 $ml \cdot kg^{-1} \cdot min^{-1}$. The heat-acclimated subjects had a mean (±SD) age of 33 ± 2 yr, body surface area of 2.0 ± 0.2 m^2, percent body fat of 20 ± 5, and maximal O_2 uptake of 50 ± 7 $ml \cdot kg^{-1} \cdot min^{-1}$. All subjects gave their voluntary and informed consent to participate in these experiments, which received approval by the appropriate Institutional Review Boards. Investigators adhered to AR 70-25 and United States Army Medical Research and Development Command Regulation 70-25 on Use of Volunteers in Research.

Protocol. For the non-heat-acclimated subjects, the experiments were conducted in the early spring months.

These subjects were members of a US Army Special Forces team whose assignment was preparation for cold-weather warfare. As a result, they trained in cold environments during the months preceding these experiments. For the heat-acclimated subjects, the experiments were conducted in the late fall-early winter months. Before the experimental days, the subjects were heat acclimated by performing treadmill exercise (0% grade at 1.34 m/s) for 120 min on 9 days in a hot-dry (45°C ambient temperature, 20% relative humidity) environment (26).

Several months before experimental testing, two units of blood were removed from each subject by phlebotomy, and a minimum of 6 wk separated the removal of each blood unit. After each phlebotomy, the blood was separated into its erythrocyte and plasma components, and the erythrocytes were frozen with 40% (wt/vol) glycerol and stored at −80°C. Immediately before infusion, the frozen cell component was thawed and washed to reduce the glycerol concentration to <1%. For infusion, the subjects received ~500 ml of a sodium chloride-glucose-phosphate solution [composed of (in g) 0.9 NaCl, 0.2 glucose, 0.0524 $NaH_2PO_4 \cdot H_2O$, and 0.1325 Na_2HPO_4 per 100 ml of solution] containing ~60% hematocrit (autologous erythrocytes). Blood volume measurements were performed several days before and 24 h after erythrocyte infusion.

The heat stress tests (HSTs) were conducted in a hot (35°C ambient temperature, 45% relative humidity) environment. This environment was selected to potentiate evaporative and limit convective and radiative heat exchange. Each HST was 120 min (2 bouts of 15-min rest and 45-min exercise) in duration. During exercise, the subjects walked (6% grade, 1.34 m/s) on a treadmill. The thermoregulatory data reported in this paper were collected during the initial 25 min of the first exercise bout. During rest and exercise, esophageal temperature, skin temperature, and local sweating rate were continuously determined. Immediately after the collection of this thermoregulatory data, O_2 uptake was measured. In addition, a venous blood sample was collected at rest and during the ~30 min of exercise.

The non-heat-acclimated subjects completed two HSTs; one was attempted ~2 wk preinfusion and the other 48 h postinfusion (23). At least 10 days separated the pre- and postinfusion HSTs to minimize any partial acclimation from the initial heat exposure. Both HSTs were attempted while the subjects were euhydrated; euhydration was determined by the achievement of a baseline body weight, which was determined from morning weighings over the preceding month. The heat-acclimated subjects completed four HSTs; two pre- (several days) and two postinfusion (48 and 96 h) (26). One HST was done while subjects were euhydrated, and the other was done while subjects were hypohydrated by 5% of body weight. Approximately 24–48 h before each hypohydration HST, the subjects voluntarily restricted food and fluid intake. Also, in the afternoon the day before the hypohydration HSTs, the subjects performed light-intensity exercise in a hot environment to dehydrate to their target body weight (5% below base line). After achieving the target body weight, the subjects were removed to a comfortable environment (T_a 20°C) to spend the night and were allowed fresh fruit and juice but only in the amounts that maintained the desired body weight. All HSTs were conducted at ~0930 h to control for any diurnal patterns.

Measurements. O_2 uptake was determined by open-circuit spirometry, with the respiratory gases collected in 150-liter Douglas bags. The volume of expired gases was measured with a Tissot gasometer, and the O_2 and CO_2 concentrations were measured with an electrochemical O_2 analyzer (Applied Electrochemistry S-3A) and an infrared CO_2 analyzer (Beckman LB-2), respectively. Skin temperatures were obtained with a three-point thermocouple skin harness (chest, calf, and upper forearm), and mean weighted skin temperature ($\bar{T}_{sk}$) was calculated. Esophageal temperature (T_{es}) was obtained from a thermistor in a catheter placed at the level of the heart, and local sweating rates ($\dot{m}_{ds}$) from the upper arm were determined by a continuously ventilated dew-point sensor placed on the skin site (10). Because the passage of saliva spuriously lowers T_{es} values (28), the subjects avoided swallowing by spitting into a cup. The threshold temperature for active thermoregulatory sweating, above that due to skin diffusion, was defined as the esophageal temperature at which the $\dot{m}_{ds}$ value achieved 0.06 mg·min^{-1}·cm^{-2} (22, 24, 25). The sweating sensitivity was defined as the slope of a regression line representing the individual minute $\dot{m}_{ds}$ and T_{es} values obtained during the initial 25-min exercise transient (22, 24, 25).

Venous blood samples were collected from an indwelling Teflon catheter placed within a superficial forearm vein. Patency was maintained with heparinized saline; the catheter (2 ml of dead space) was flushed with 4 ml of blood before each 8-ml sample was obtained. Blood samples taken at rest were obtained after the subjects had stood quietly for 20 min in the antechamber (20°C T_a, 40% rh), and exercise blood samples were taken during exercise while the subjects continued to walk. All blood samples were obtained with the catheterized arm hanging in a relaxed manner over the handrail of the treadmill. Triplicate measurements of all blood variables were made. An automated system was used to measure hemoglobin (Hemoglobinometer, Coulter Electronics), and plasma osmolality was measured by a vapor pressure osmometer (model 5500, Wescor). Plasma volume and erythrocyte volume at rest (euhydrated) were measured by the ^{125}I-labeled albumin method and the ^{51}Cr method (32), respectively. The percent changes in plasma volume were calculated from the appropriate hemoglobin and hematocrit values (4). The absolute plasma volumes during exercise were calculated by adjusting the measured resting plasma volume by the appropriate percent change in plasma volume. Blood volume was calculated as the sum of plasma volume and erythrocyte volume.

Statistical analyses. Means ± SD, simple and multiple regression, and analysis of variance (ANOVA) for repeated and nonrepeated measures were calculated. Statistical significance was tested at the $P < 0.05$ level.

RESULTS

To evaluate the effects of erythrocyte infusion on physiological responses, two separate ANOVAs were per-

formed for each variable. The first ANOVA examined the effects of erythrocyte infusion for euhydrated individuals who were either non-heat acclimated ($n = 6$) or heat acclimated ($n = 5$). The second ANOVA examined the effects of erythrocyte infusion for heat-acclimated individuals ($n = 3$) as well as the effects of hydration (euhydrated or hypohydrated). Note that three data sets were employed for the second ANOVA, because two subjects were unable to swallow the esophageal catheter during the preinfusion hypohydration experiments.

Table 1 provides the metabolic rate and thermoregulatory control responses during exercise in the heat. Metabolic rate was not altered by erythrocyte infusion as well as hydration status. Erythrocyte infusion did not decrease ($P = 0.08$) threshold temperature for the unacclimated subjects, but the heat-acclimated subjects decreased ($P < 0.01$) their threshold temperature (mean of eu- and hypohydration conditions) by 0.28°C after infusion. Hypohydration did not statistically alter threshold temperature for thermoregulatory sweating because the large preinfusion increase (eu- to hypohydration) was offset by the large effects of erythrocyte infusion. Erythrocyte infusion increased ($P < 0.01$) sweating sensitivity by 78% for the unacclimated subjects and by 46% (mean of eu- and hypohydration conditions) for the heat-acclimated subjects. Hypohydration decreased ($P < 0.05$) sweating sensitivity by 17%. Figure 1 illustrates all of the individual data for the effects of erythrocyte infusion on threshold temperature and sweating intensity. Note that 11 of 14 threshold temperature values were decreased (below the line of identity), and all sweating sensitivity values were increased (above the line of identity) after erythrocyte infusion.

Table 2 provides the plasma osmolality and blood volume data for subjects during rest and exercise-heat stress. Erythrocyte infusion did not alter plasma osmolality for the unacclimated subjects, but the heat-acclimated subjects decreased ($P < 0.05$) their plasma osmolality after infusion. Hypohydration increased ($P < 0.01$) plasma osmolality for the heat-acclimated subjects. Erythrocyte infusion did not alter blood volume for the unacclimated subjects, but the heat-acclimated subjects increased ($P < 0.01$) their blood volume after infusion. Hypohydration did not statistically alter blood volume.

TABLE 1. *Metabolic rate and thermoregulatory control responses to exercise-heat stress*

Subject Status	n	Aerobic Metabolic Rate, $W \cdot m^{-2}$	Sweating Threshold Temperature, °C	Sweating Sensitivity, $mg \cdot cm^{-2} \cdot min^{-1} \cdot K^{-1}$	
Unacclimated subjects					
Euhydrated					
Preinfusion	6	358±25	36.96±0.34	0.36±0.13	*
Postinfusion	6	349±28	36.87±0.34	0.64±0.16	*
Acclimated subjects					
Euhydrated					
Preinfusion	5	322±22	36.53±0.06	0.50±0.06	* †
Postinfusion	5	325±20	36.47±0.15	0.80±0.05	* †
Hypohydrated					
Preinfusion	3	325±20	37.11±0.17	0.44±0.08	* †
Postinfusion	3	319±18	36.62±0.34	0.65±0.08	* †

Values are means ± SD, n = no. of subjects. Data are significant at * $P < 0.05$ (infusion) and † $P < 0.05$ (hydration).

To determine the influence of plasma osmolality and blood volume on the control of thermoregulatory sweating, the individual changes in plasma osmolality and individual changes in blood volume relative to control conditions (euhydration, preinfusion) were calculated. Regression analyses were performed to determine the relationships between the individual changes (compared with euhydration, preinfusion) in these hematologic variables to the individual threshold temperature shifts and individual sweating sensitivity changes (compared with euhydration, preinfusion). The threshold temperature shifts were related to the changes in plasma osmolality (exercise values; $r = 0.85$, $P < 0.01$) as well as with the changes in blood volume (preexercise values; $r = -0.75$, $P < 0.01$); the individual values are depicted in Fig. 2. Note that each data point represents the comparison of two separate experiments. The threshold temperature shifts (compared with euhydration, preinfusion) were best described by the equation

$$\Delta Th = 0.03550(\Delta osmol_{ex}) - 0.01351(\Delta BV_r) - 0.03609$$

($r = 0.87$, $P < 0.01$) where ΔTh (°C) is the change in threshold temperature for thermoregulatory sweating, $\Delta osmol_{ex}$ (mosmol/kg) is the change in osmolality (exercise values), and ΔBV_r (%) is the change in blood volume (preexercise values).

The sweating sensitivity changes were related to the changes in blood volume (exercise values; $r = 0.53$, $P < 0.05$) as well as with the changes in osmolality (preexercise values; $r = -0.49$, $P < 0.05$). The sweating sensitivity changes (compared with euhydration, preinfusion) were best described by the equation

$$\Delta SS = 0.01381(\Delta BV_{ex}) + 0.00718(\Delta osmol_r) + 0.27038$$

($r = 0.55$, $P < 0.05$) where ΔSS ($mg \cdot cm^{-2} \cdot min^{-1} \cdot K^{-1}$) is the change in sweating sensitivity, ΔBV_{ex} (%) is the change in blood volume (exercise values), and $\Delta osmol_r$ (mosmol/kg) is the change in osmolality (preexercise values).

DISCUSSION

Body temperature is believed to be regulated by a proportional control system (9, 14, 28). A proportional system is defined as the graded response of a controlled variable (e.g., sweating) to the displacement of the regulated variable (e.g., body temperature). Both peripheral and central thermal receptors provide afferent input into the hypothalamic thermoregulatory centers where this information is processed with a resultant effector signal to initiate and maintain sweating rate (9, 14, 28). For humans, $\bar{T}_{sk}$ provides an index of peripheral thermal information and T_{es} provides an index of central thermal information affecting sweating with relative weightings of 0.1 and 0.9, respectively (19). In our analyses, we used T_{es} as the index of thermal drive for sweating because the local and mean skin temperature values were not altered by any of the experimental conditions (23, 26).

Erythrocyte infusion generally decreased the threshold temperature for thermoregulatory sweating and always

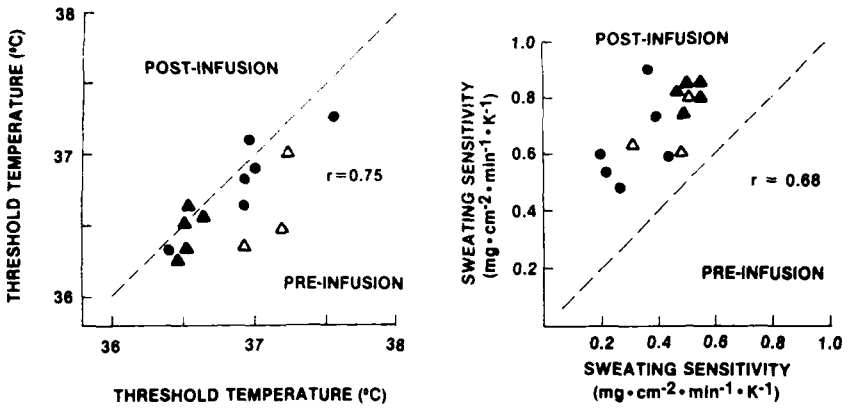

FIG. 1. Individual data for threshold temperature and sweating sensitivity responses to pre- and postinfusion heat stress tests. Broken line, line of identity. Filled circles, euhydrated non-heat-acclimated subjects; filled triangles, euhydrated heat-acclimated subjects; open triangles, hypohydrated heat-acclimated subjects.

TABLE 2. *Plasma osmolality and blood volume values during rest and exercise-heat stress*

Subject Status	n	Plasma Osmolality, mosmol/kg		Blood Volume, l	
		Rest	Exercise	Rest	Exercise
Unacclimated subjects					
Euhydrated					
Preinfusion	6	285±2	288±2	5.61±0.40	5.89±0.45
Postinfusion	6	287±3	288±3	5.60±0.52	5.94±0.49
Acclimated subjects					
Euhydrated					
Preinfusion	5	283±3	287±2 *†	5.35±0.59	5.40±0.66 *
Postinfusion	5	283±1	284±2 *†	5.62±0.72	5.82±0.71 *
Hypohydrated					
Preinfusion	3	300±2	302±4 *	4.72±0.01	4.92±0.26 *
Postinfusion	3	296±3	296±3 *	4.89±0.52	5.25±0.17 *

Values are means ± SD. n = no. of subjects. Data are significant at * $P < 0.05$ (infusion) and † $P < 0.05$ (hydration).

increased the sweating sensitivity during moderate-intensity exercise in the heat. The decrease in threshold temperature was modest for the euhydrated subjects but was striking for the hypohydrated subjects after erythrocyte infusion. Conversely, sweating sensitivity values were always markedly increased by erythrocyte infusion regardless of the subject's hydration status. Both a decreased threshold temperature and an increased sweating sensitivity indicate an improved thermoregulatory sweating response to exercise-heat after erythrocyte infusion.

The most significant finding is that the thermoregulatory control parameters of threshold temperature for sweating and sweating sensitivity can be improved beyond those levels observed for an individual with a normal plasma tonicity and blood volume. We are not familiar with other research demonstrating these same results; however, one study (7) has reported that acute hypervolemia (9% expansion of blood volume) lowered core temperature values during exercise despite no change in the thermoregulatory control parameters of threshold temperature and sweating sensitivity. Those experiments were conducted in a 30°C environment, so it is possible that the hypervolemia may have mediated an increased skin blood flow and dry heat loss to account for lowered core temperature values (7). Other investigators (6, 18, 27) have found that acute hypervolemia does not provide a thermoregulatory advantage compared with normovolemia during exercise in the heat. Several investigators (5, 13, 17, 20, 21) have examined the effects of excessive fluid ingestion or hyperhydration on thermoregulatory responses during exercise in the heat. Some of the investigators reported that hyperhydration resulted in an increased total body sweating rate (17) and reduced core temperature (17, 21) during exercise in the heat. Other investigators, however, have reported

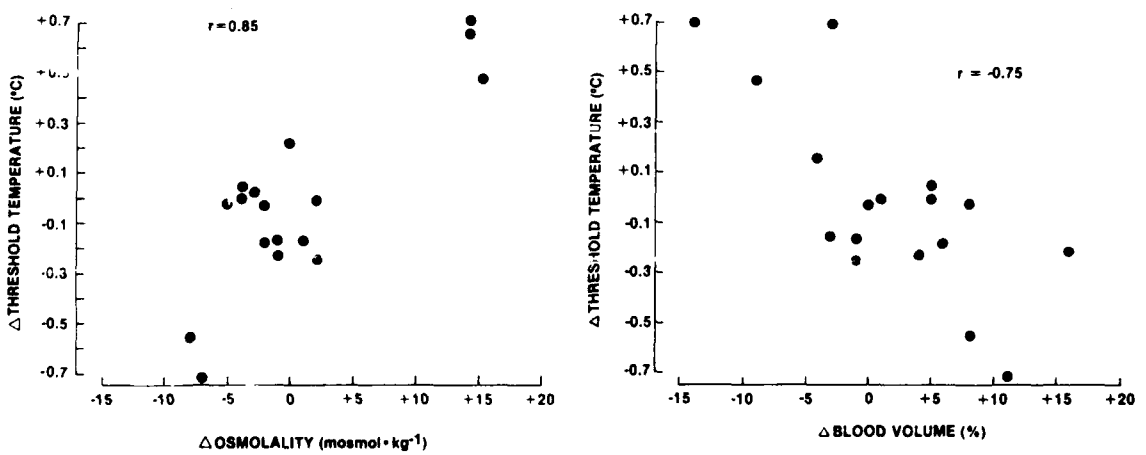

FIG. 2. Individual data for change (Δ, compared with euhydration, preinfusion) in relationship of threshold temperature to change in plasma osmolality (exercise values) and change in blood volume (preexercise values).

that hyperhydration did not provide a thermoregulatory advantage (3, 11) or that it reduced core temperature with no change in total body sweating (13) during exercise in the heat.

When the present experiments are compared with previous hypervolemia-hyperhydration investigations, several important factors must be considered. First, the erythrocyte infusion elicited a hypervolemia that was fairly long term (at least 48–96 h), unlike previous studies in which blood volume was acutely expanded immediately before the exercise-heat exposure (7, 8, 13, 18, 21, 27). It is possible that hypervolemia is required for several hours to readjust the cardiovascular system (via the baroreceptor reflex) so that the thermoregulatory sweating can be enhanced. Second, in this study plasma tonicity (particularly the exercise values) and blood volume often changed in concert, so that a potentiating effect may have occurred that was greater than if each were altered independently of the other. Third, we evaluated thermoregulatory sweating in a more precise manner than some of the previous hyperhydration-hypervolemia studies that only examined total body sweating (11, 13, 17, 21, 27).

The threshold temperature for thermoregulatory sweating can be shifted above or below control levels dependent on both changes in plasma tonicity and blood volume (Fig. 2), and plasma tonicity changes accounted for a considerable amount of variance (72%) in threshold temperature shifts. A threshold temperature shift is often interpreted as indicative of a central nervous system-mediated change in the thermoregulatory effector signal (28). The plasma tonicity changes, as measured in this study, may correlate with tonicity changes in the extracellular fluid bathing the hypothalamic neurons (16, 21). Silva and Boulant (31) have demonstrated that in rat brain slices, there are preoptic anterior hypothalamic neurons that are both thermosensitive and osmosensitive. Therefore, these data indicate a central interaction between thermoregulation and body water regulation. Numerous other animal studies have demonstrated that the intravascular (1, 2, 12, 16) or intracranial (5) infusion of hypertonic solutions elevates core temperature during rest and exercise in the heat. Several human studies have demonstrated that the ingestion of hypertonic fluid elevates core temperature responses in the heat, despite the maintenance of euhydration (15, 20, 21). Consistent with this, in humans an inverse relationship ($r = -0.62$ to -0.76) between plasma osmolality and total body sweating has been reported by several investigators (29, 30). Similarly, Fortney et al. (8) have reported that hyperosmolality increases the threshold temperatures for sweating and cutaneous vasodilation even without a blood volume reduction during exercise in the heat. The combined results of these studies indicate that plasma osmolality exerts a powerful influence on thermoregulatory sweating and body temperature responses to exercise and heat stress.

Sweating sensitivity can also be increased or decreased relative to control levels (when normal blood volume and plasma tonicity are present), with changes in blood volume accounting for a substantial amount of variance (28%) for the change in sweating sensitivity. Sweating sensitivity changes are generally interpreted to indicate a peripheral effect localized at the individual eccrine sweat gland (9, 19, 28), but others (7, 25) have suggested that sweating sensitivity changes could reflect a central nervous system-mediated alteration. For example, hypovolemia and hypervolemia either unload or load the low-pressure baroreceptors. Fortney et al. (7) have suggested that hypovolemia may alter the activity of atrial baroreceptors that could have afferent input to the hypothalamic thermoregulatory centers. Therefore, a peripheral input could result in a central nervous system-mediated alteration in sweating sensitivity. Those investigators also reported that an isotonic hypovolemia (9% reduction in blood volume) reduced the sweating sensitivity by 42% from control levels. If sweating sensitivity changes do represent a peripheral effect, the increased plasma tonicity may also have exerted its influence via a high interstitial osmotic pressure inhibiting the fluid availability to the eccrine sweat gland (11, 21).

Our findings concerning thermoregulatory sweating during exercise in the heat are summarized as follows: *1*) acute polycythemia decreases the threshold temperature and increases the sweating sensitivity; *2*) both threshold temperature and sweating sensitivity are increased or decreased from control levels (when normal plasma tonicity and blood volume are present) dependent on the combined influence of plasma tonicity and blood volume; and *3*) equations are presented that describe how plasma tonicity and blood volume alter threshold temperatures and sweating sensitivity values. Homeostatically, our findings are logical in that when an individual has an abundance of body water, it is employed to increase evaporative cooling and defend body temperature during exercise in the heat; conversely, when there is a shortage of body water, it is conserved to maintain cardiovascular stability. During the hypohydrated state, the strategy may be that the reduced sweating that mediates a higher core temperature elicits behavioral thermoregulatory actions to reduce the exercise intensity and remove the heat stress.

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